Editorials

Polychlorinated Biphenyls Revisited

DR GIDEON LETZ in this issue presents a summary of the toxicology of polychlorinated biphenyls (PCB's) for clinicians. This overview illustrates the usual dilemma we find ourselves in. The animal data suggest that PCB's affect the immune response and are fetotoxic and carcinogenic. In humans they have been shown to cause chloracne, and they may affect serum lipid levels and liver function, but, thus far, the possible effects on the immune system and on reproduction have not really been studied. Our attempts to determine whether these chemicals produce cancer in humans have, at best, been inadequate, but our dilemma goes even further.

In the first half of this century, not much attention was paid to chronic toxicity. If a chemical such as PCB had almost no acute toxicity, it was considered safe. It was not until Jensen, in 1966 in Sweden, found PCB's in the environment and then the first *Yusho* outbreak in 1968 that concerns about PCB's were voiced.

These chemicals were found to have spread extensively through the environment in the United States and other parts of the industrialized world. They were present in some of our foods, particularly fish, but also in cereal, eggs, poultry, meat and milk. How did they get there? Industry was not very careful in containing PCB's, which, in turn, led to contamination of rivers and lakes and, thus, fish. In the 1960s, PCB's were used in carbonless copying paper which was recycled and made into cereal boxes. The PCB's then migrated from the cereal boxes into the cereal. PCB's had many open-ended uses—for example, as additives in paints used on silos and as heat exchangers in feed processing operations. Through this use animal feed became contaminated. Such open-ended uses were discontinued in 1971 in the United States, and after the Toxic Substances Act was passed in 1976, the use of PCB's elsewhere has been gradually phased out. But, as the author points out, about half of the PCB's ever made are still in transformers and capacitors, and they continue to present an enormous management and disposal problem.

In addition to the environmental contamination, the general population was found to have body burdens of PCB's. Since PCB's are lipid soluble, they are primarily stored in adipose tissue. To a lesser extent, they are present in serum and some organs. They are also excreted in human milk. It is not known whether trace amounts of these chemicals at concentrations of a few milligrams per kilogram in adipose tissue or of a few nanograms per milliliter in serum have any impact on human health.

In the past, it has always been assumed that with exposure being constant a steady state is eventually reached where intake and excretion go into a balance and PCB's no longer build up in tissues. Since some of the PCB isomers are extremely persistent with a very long biological half-life, it is not clear whether or when this steady state would ever be reached during the average life span of the human being. It is now also apparent that some isomers in this PCB mixture are much more persistent and toxic than others, and it seems that the more toxic isomers are relatively bioconcentrated in the environment. Thus, PCB's that have passed through the environment may not be the same PCB's to which workers are exposed.

Once toxic effects have been observed in animals, the health of workers exposed to similar chemicals is usually reviewed. If these workers are found to be healthy, the animal data are immediately questioned. Perhaps we should first examine to what extent the human data are adequate and useful. As Dr Letz points out, too few workers have been examined, and their length of exposure has been too short to address the question of carcinogenic properties of PCB's. Furthermore, workers are exposed to the original commercial mixture, but the general population is exposed to a possibly more toxic mixture that has been modified by the environment. In addition, older workers have not been exposed to these chemicals during their childhood and in utero, but the younger members of the general population have been so exposed.

Because these chemicals are extremely persistent and because they do have chronic toxic effects in animals and are carcinogenic in rodents, it is only prudent to reduce human exposure to them as much as possible. It would not be in the interest of public health to wait for the carcinogenic or reproductive effects to be shown in humans. Once that point is reached, it would be too late to take preventive measures. It may not be possible to determine in individual cases whether PCB exposure has resulted in health effects, since such effects, with the exception of chloracne, are nonspecific. But, as Dr Letz points out, that should not deter us from seeking to reduce exposure to these agents.

RENATE D. KIMBROUGH, MD
Medical Officer
Center for Environmental Health
Centers for Disease Control
Atlanta

Medicine in a Forest of Thickets and Trees

IN MANY WAYS physicians, and indeed the medical profession as a group, seem to be trying to find their way through what might be compared to a rather dense forest with many formidable trees. Moreover the forest is also full of thickets. The thickets are the administrative and bureaucratic frustrations in a physician's daily practice; in a different dimension, they often impede

or thwart organizational goals of the profession in behalf of patients and the public. The trees are the larger and more generic problems with which both practitioners and the profession as a whole must deal. They include such troublesome things as the endless rules and regulations imposed by often well-intentioned but poorly constructed laws, rising health care costs that no one wants any longer to pay, confusing signals about competition in medical practice and patient care, new kinds of relatively untried health care and practice plans that may or may not contain booby traps for physicians or their patients, many kinds of expensive and often wasteful litigation that seem to benefit lawyers more than anyone else—only to mention a few. It is easy for physicians and the profession to feel confused, frustrated and powerless while trying to find a path through a forest of thickets and trees such as these.

But in this forest other powerful forces are at work. It is clear that irreversible changes are taking place in health care. The force that drives these changes is progress in medical science and technology. The social, economic, political and human impact of this progress is unprecedented and has created new kinds of problems with which we do not yet know how to deal. Society wants access to the best of health care and, yes, health for all. The sophisticated health care personnel, equipment and facilities needed for this are proving to be overwhelmingly costly. Yet health and health care are national goals strongly supported by the public and this is important politically. And advancing medical science and technology have given rise to an array of ethical and legal issues that have important but as yet unresolved social, economic and political ramifications. It is more and more apparent that a genuinely new technologic, social, economic, political and even human interdependence may be emerging in the area of health care.

In the health care enterprise there are actually many autonomous and independent units which are nevertheless interdependent. And nothing is constant in health care. Everything is changing all the time, even while it is being studied. All this seems to resemble something like a biologic system with its relatively independent yet interdependent cells and organ systems that must and do interact with ever changing internal and external environments. If this is true it is little wonder that the American health care system is poorly understood, since it does not fit easily into the established social, economic and political stereotypes which are better adapted to dealing with simpler and more stable systems. Could this forest, with its thickets and trees, actually be a quasi-living system with many of the characteristics of more familiar biologic systems?

If there is any reality to this analogy, the path for physicians and the medical profession in this forest begins to become clearer. In patient care physicians have developed effective methods of diagnosing and treating the ailments of a living, changing human organism. The principles of chief complaint, present illness, past history, social history, system review, physical examination, collection of objective data by laboratory and other methods, consultation with specialists in different fields when needed, a working diagnosis, plan of treatment, informed consent, agreement on what is to be done and by whom, institution of treatment program, monitoring for progress and change then making corrections to refine the diagnosis and treatment during changes in the course of the illness until the problem is solved or a steady state is reached, are principles taught to every medical student.

If the health care system indeed to some extent resembles a quasi-living organism, perhaps it is time for the medical profession to seek ways to work within the health care system that will enable it to apply some of the principles learned in medical school to the diagnosis and treatment of the ailments of this quasi-living system. At the very least some clearings might begin to be made in this forest of thickets and trees.

—MSMW

Reflections on Stones

A PRACTICAL REVIEW of how to treat renal stones, such as the Specialty Conference elsewhere in this issue, properly emphasizes that disordered urine chemistry causes unwanted crystal formation. There seem to be four mechanisms for stone formation and they are unequally important, at least at the moment. Overexcretion is the clearest one, illustrated by idiopathic hypercalciuria, primary hyperparathyroidism, hyperoxaluria and cystinuria. In each of these conditions, excessive amounts of insoluble materials are present in the urine and raise supersaturation unless a higher urine volume offsets the increased excretion rate.

Alternatively, abnormalities of urine chemistry can create conditions such that even normal excretion rates will result in supersaturation, and this is a more subtle problem. For example, low urine pH causes urine to become excessively supersaturated with respect to undissociated uric acid in patients who have gout or familial uric acid nephrolithiasis, even in the absence of hyperuricosuria.[1] On the other hand, an elevated urine pH near that of blood, as may occur in distal renal tubular acidosis, promotes the crystallization of calcium phosphate minerals even when hypercalciuria is of modest degree or absent altogether.[2] Bacteria that possess urease raise urine pH to near 9, and under this condition magnesium ammonium phosphate (struvite) can form spontaneously, especially because the organisms raise urinary ammonium content as well as pH.

A third mechanism is that of crystal-crystal interaction. At the moment, the only example of this—and not altogether proved—is in hyperuricosuric calcium oxalate stone disease. In this condition, a high intake of meat, fish and poultry lowers urine pH modestly and causes hyperuricosuria; the combination raises urine supersaturation with respect to undissociated uric